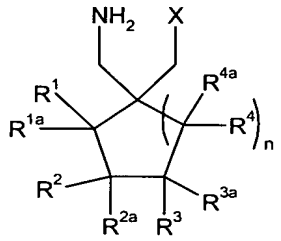
CLAIMS

1. A method of treating COPD or a disease, disorder or condition associated with a diagnosis of COPD in a mammal, which method comprises administering to said mammal in need of such treatment a therapeutically effective amount of a compound comprising an alpha-2-delta ligand or a pharmaceutically acceptable salt thereof.

2. The method of claim 1 wherein the alpha-2-delta ligand is a compound of formula (I),



(I)

,

wherein:

X is a carboxylic acid or carboxylic acid bioisostere;

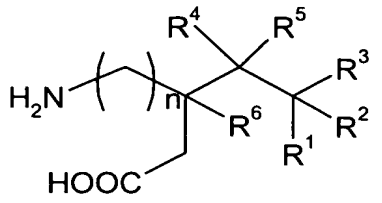
n is 0, 1 or 2; and

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4 and R^{4a} are independently selected from H and C_1-C_6 alkyl, or

R^1 and R^2 or R^2 and R^3 are taken together with the carbon atoms to which they are attached to form a C_3-C_7 cycloalkyl ring, which ring is optionally substituted with one or two C_1-C_6 alkyl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

3. The method of claim 2 wherein the alpha-2-delta ligand compound is 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one; [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid; (3S,4S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid; or (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, a stereoisomer or prodrug prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

4. The method of claim 1 wherein the alpha-2-delta ligand is a compound of formula (II),



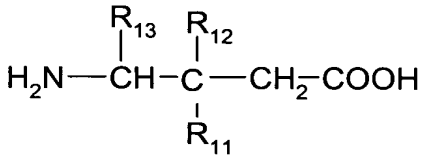
(II),

wherein:

n is 0 or 1,

R^1, R^2, R^3, R^4, R^5, and R^6 are independently H or C_1-C_6 alkyl;

with the proviso that compounds of formula (IIa) are excluded:

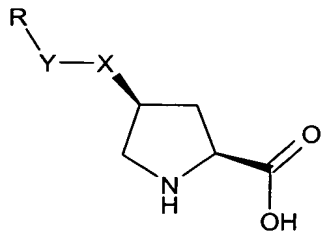


(IIa)

wherein R_{11} is a straight or branched alkyl of from 1 to 6 carbons, phenyl, or cycloalkyl having from 3 to 6 carbon atoms; R_{12} is hydrogen or methyl; and R_{13} is hydrogen methyl or carboxyl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

5. The method of claim 4 wherein the alpha-2-delta ligand compound is (3S,5R)-3-aminomethyl-5-methyl-octanoic acid; (3S,5R)-3-amino-5-methyl-heptanoic acid; (3S,5R)-3-amino-5-methyl-nonanoic acid; or (3S,5R)-3-amino-5-methyl-octanoic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

6. The method of claim 1 wherein the alpha-2-delta ligand is a compound of formula (III),



(III),

wherein:

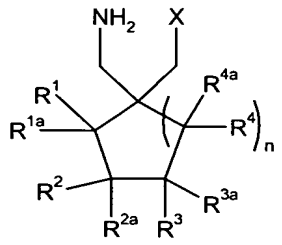
either (a) X is O, S, NH or CH_2 and Y is CH_2 or a direct bond; or (b) Y is O, S or NH and X is CH_2; and

R is a 3-12 membered cycloalkyl, 4-12 membered heterocycloalkyl, aryl or heteroaryl, where any ring may be optionally substituted independently with one or more halogen, hydroxy, cyano, nitro, amino, hydroxycarbonyl, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, C_1-C_6 alkoxy, hydroxyC_1-C_6 alkyl, C_1-C_6 alkoxyC_1-C_6 alkyl, perfluoro C_1-C_6 alkyl, perfluoroC_1-C_6 alkoxy, C_1-C_6 alkylamino, di- C_1-C_6 alkylamino, aminoC_1-C_6 alkyl, C_1-C_6 alkylaminoC_1-C_6 alkyl, di-C_1-C_6 alkylaminoC_1-C_6 alkyl, C_1-C_6acyl, C_1-C_6acyloxy, C_1-C_6acyloxyC_1-C_6 alkyl, C_1-C_6 acylamino, C_1-C_6 alkylthio, C_1-C_6 alkylthiocarbonyl, C_1-C_6 alkylthioxo, C_1-C_6 alkoxycarbonyl, C_1-C_6 alkylsulfonyl, C_1-C_6 alkylsulfonylamino, aminosulfonyl, C_1-C_6 alkylaminosulfonyl, di-C_1-C_6 alkylaminosulfonyl, 3-8 membered cycloalkyl, 4-8 membered heterocycloalkyl, phenyl and monocyclic heteroaryl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

7. The method of claim 6 wherein the alpha-2-delta ligand is (2S, 4S)-4-(3-chloro-phenoxy)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(3-fluoro-benzyl)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(2,3-difluoro-benzyl)-pyrrolidine-2-carboxylic acid; or (2*S*,4*S*)-4-(3-fluoro-phenoxymethyl)-pyrrolidine-2-carboxylic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

8. A method of treating chronic cough in a mammal, which method comprises administering to said mammal in need of such treatment a therapeutically effective amount of an alpha-2-delta ligand, or a pharmaceutically acceptable salt thereof.

9. The method of claim 8 wherein the alpha-2-delta ligand is a compound of formula (I),



(I) ,

wherein:

X is a carboxylic acid or carboxylic acid bioisostere;

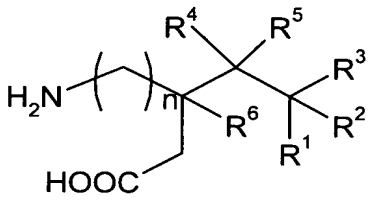
n is 0, 1 or 2; and

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4 and R^{4a} are independently selected from H and C_1-C_6 alkyl, or

R^1 and R^2 or R^2 and R^3 are taken together with the carbon atoms to which they are attached to form a C_3-C_7 cycloalkyl ring, which ring is optionally substituted with one or two C_1-C_6 alkyl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

10. The method of claim 9 wherein the alpha-2-delta ligand compound is selected from 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one; [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid; (3S,4S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid; or (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

11. The method of claim 8 wherein the alpha-2-delta ligand is a compound of formula (II),



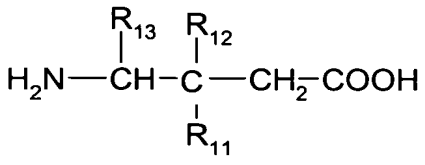
(II) ,

wherein:

n is 0 or 1,

R^1, R^2, R^3, R^4, R^5, and R^6 are independently H or C_1-C_6 alkyl;

with the proviso that compounds of formula (IIa) are excluded:

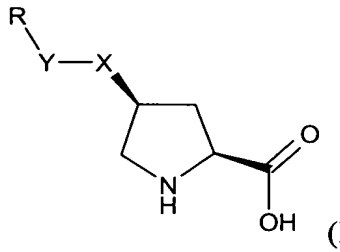


(IIa)

wherein R_{11} is a straight or branched alkyl of from 1 to 6 carbons, phenyl, or cycloalkyl having from 3 to 6 carbon atoms; R_{12} is hydrogen or methyl; and R_{13} is hydrogen methyl or carboxyl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

12. The method of claim 11 wherein the alpha-2-delta ligand compound is (3S,5R)-3-aminomethyl-5-methyl-octanoic acid; (3S,5R)-3-amino-5-methyl-heptanoic acid; (3S,5R)-3-amino-5-methyl-nonanoic acid; or (3S,5R)-3-amino-5-methyl-octanoic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

13. The method of claim 8 wherein the alpha-2-delta ligand is a compound of formula (III),



(III),

wherein:

either (a) X is O, S, NH or CH_2 and Y is CH_2 or a direct bond; or (b) Y is O, S or NH and X is CH_2; and

R is a 3-12 membered cycloalkyl, 4-12 membered heterocycloalkyl, aryl or heteroaryl, where any ring may be optionally substituted independently with one or more halogen, hydroxy, cyano, nitro, amino, hydroxycarbonyl, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, C_1-C_6 alkoxy, hydroxyC_1-C_6 alkyl, C_1-C_6 alkoxyC_1-C_6 alkyl, perfluoro C_1-C_6 alkyl, perfluoroC_1-C_6 alkoxy, C_1-C_6 alkylamino, di- C_1-C_6 alkylamino, aminoC_1-C_6 alkyl, C_1-C_6 alkylaminoC_1-C_6 alkyl, di-C_1-C_6 alkylaminoC_1-C_6 alkyl, C_1-C_6acyl, C_1-C_6acyloxy, C_1-

C_6acyloxyC_1-C_6 alkyl, C_1-C_6 acylamino, C_1-C_6 alkylthio, C_1-C_6 alkylthiocarbonyl, C_1-C_6 alkylthioxo, C_1-C_6 alkoxycarbonyl, C_1-C_6 alkylsulfonyl, C_1-C_6 alkylsulfonylamino, aminosulfonyl, C_1-C_6 alkylaminosulfonyl, di-C_1-C_6 alkylaminosulfonyl, 3-8 membered cycloalkyl, 4-8 membered heterocycloalkyl, phenyl and monocyclic heteroaryl; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

14. The method of claim 13 wherein the alpha-2-delta ligand is (2S, 4S)-4-(3-chloro-phenoxy)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(3-fluoro-benzyl)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(2,3-difluoro-benzyl)-pyrrolidine-2-carboxylic acid; or (2*S*,4*S*)-4-(3-fluoro-phenoxymethyl)-pyrrolidine-2-carboxylic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug.

15. The method of any one of claims 1 - 7 wherein said COPD is the COPD that includes chronic bronchitis, pulmonary emphysema or dyspnea associated therewith, or said COPD is characterized by irrerversible, progressive airways obstruction, adult respiratory distress syndrome (ARDS) or exacerbation of airways hyper-reactivity consequent to other drug therapy.

16. The method of either claim 1 or 8, wherein the alpha-2-delta ligand compound is gabapentin; pregabalin; [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid; 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one; (3S,4S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid; (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid; (3S,5R)-3-aminomethyl-5-methyl-octanoic acid; (3S,5R)-3-amino-5-methyl-heptanoic acid; (3S,5R)-3-amino-5-methyl-nonanoic acid; (3S,5R)-3-amino-5-methyl-octanoic acid; (2S, 4S)-4-(3-Chloro-phenoxy)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(3-fluoro-benzyl)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(2,3-difluoro-benzyl)-pyrrolidine-2-carboxylic acid; or (2*S*,4*S*)-4-(3-fluoro-phenoxymethyl)-pyrrolidine-2-carboxylic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer, or prodrug.

17. The method of claim 16 wherein the alpha-2-delta ligand compound comprises (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer, or prodrug.

18. The method of claim 15 wherein the alpha-2-delta ligand compound is gabapentin; pregabalin; [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid; 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one; (3S,4S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid; (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid; (3S,5R)-3-aminomethyl-5-methyl-octanoic acid; (3S,5R)-3-amino-5-methyl-heptanoic acid; (3S,5R)-3-amino-5-methyl-nonanoic acid; (3S,5R)-3-amino-5-methyl-octanoic acid; (2S, 4S)-4-(3-Chloro-phenoxy)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(3-fluoro-benzyl)-pyrrolidine-2-carboxylic acid; (2*S*,4*S*)-4-(2,3-difluoro-benzyl)-pyrrolidine-2-carboxylic acid; or (2*S*,4*S*)-4-(3-fluoro-phenoxymethyl)-pyrrolidine-2-carboxylic acid; a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer, or prodrug.

19. The method of claim 18 wherein the alpha-2-delta ligand compound comprises (1α,3α,5α)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer, or prodrug.

20. A method of treating COPD or a disease, disorder or condition associated with a diagnosis of COPD in a mammal, which method comprises administering to said mammal in need of such treatment a pharmaceutical composition comprising an alpha-2-delta ligand, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, vehicle or diluent.

21. A method of treating chronic cough in a mammal, which method comprises administering to said mammal in need of such treatment a pharmaceutical composition comprising an alpha-2-delta ligand, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, vehicle or diluent.